Isolated sudden onset anosmia in COVID-19 infection. A novel syndrome?*

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Introduction

There are three well described syndromes in the current SARS-CoV-2 outbreak: asymptomatic, mild URTI, and severe systemic disease such as bilateral interstitial pneumonia [(1)]. We and many others have noticed a sudden increase in presentations of an otherwise asymptomatic anosmia during the early stages of the pandemic within the UK population. This correlates with personal communication reports from colleagues in Italy and China. We present a case report of one confirmed COVID-19 positive patient with supporting evidence for a fourth syndrome of this viral infection, namely Isolated Sudden-Onset Anosmia (ISOA).

Case report

A 48-year-old neurosurgeon presented for telephone consultation with a sudden onset of complete anosmia over seventy two hours without any other symptoms. He was otherwise fit and well, with no comorbidities and a normal BMI. Based on the suspicions from anecdotal reports from other countries, he was advised to self-isolate. He did not develop any further symptoms but underwent PCR testing two days later, confirming SARS-CoV-2 infection. He remains otherwise asymptomatic to date (six days since presentation).

Other evidence

In the absence of a gold standard confirmed COVID-19+ testing in an otherwise isolated sudden onset anosmia, the other evidence is circumstantial: the increase in reported and referred sudden anosmia correlating with the number of diagnosed cases of SARS-CoV-2 in the early days of the pandemic within the UK, reports on social media and the increase in searches for the topic on search engines correlating with case numbers. One of the authors has experienced a nine-fold increase in referrals for sudden onset, otherwise asymptomatic, anosmia in her rhinology practice over the last three weeks. The presentation in all of these cases is the same: complete subjective loss of smell and taste over 24 to 72 hours without other significant symptoms of an URTI.

There is now a well-recognised association of anosmia with SARS-CoV-2 in the current pandemic with multiple reports of smell loss with the infection. For instance, the UK smell training charity AbScent has experienced a four-fold increase in Facebook membership over the last two months (Figure1), and a 77.3% increase in website use, mainly concentrating on the pages to do with smell loss and COVID-19.

Admittedly, these changes may reflect only an increase in the overall anosmia related to the pandemic, and not the sudden isolated anosmia syndrome. There are, however, numerous patient reports on social media of smell loss only, albeit none clinically verified as yet. A recent (24 March 2020) poll of the members of the AbScent anosmia Facebook group found out of a total of 49 who had lost their sense of smell in the last two months, 19 had no other symptoms, a base rate significantly higher than the usual monthly membership. This may be explained by the increase in overall awareness around smell loss due to the press around anosmia in conjunction with COVID-19 but is supportive of our hypothesis.

Similarly a search for the "anosmia" topic on Google Trends (https://trends.google.com/trends/) shows an unprecedented increase in searches in the countries as they are reached by the spread of the virus (Figure 2), indicating the association of anosmia with the infection. In Figure 2, the Italian searches predate those in the US and the UK as is demonstrated. Again, this does not support an ISOA syndrome but does support a strong association of anosmia with the disease.

Table 1 presents a case series of patients presenting to the clinical authors with either ISOA or isolated anosmia as a prodromal symptom preceding a full URTI syndrome. All of these presented before the ENT-UK paper on smell loss as a presenting symptom of COVID-19 [(2)] was released. Unfortunately, only one, presented above, was able to obtain testing for SARS-CoV-2 infection.

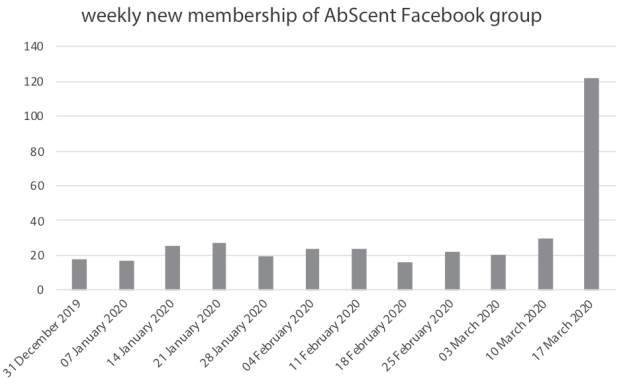

Figure 1. Week y new membership numbers of AbScent Face Book group showing unprecedented four-fold increase in mid-March as UK pandemie arrived.

Aetiology

In the absence of full objective smell assessment and nasendoscopy (contraindicated in the current situation) the precise aetiology of this syndrome remains undetermined. Two possibilities seem likely: olfactory cleft syndrome [3] with mucosal obstruction of the olfactory cleft and a "conductive" loss, or a post-viral anosmia syndrome with direct infection of the olfactory mucosa and destruction of the olfactory sensory neurons: a "neural" loss. These syndromes have different outcomes, in the olfactory cleft syndrome we would expect a relatively rapid return of normal olfaction with the resolution of any other nasal symptoms. In the "neural" case, recovery would be prolonged and with a higher chance of persistent olfactory deficit.

Treatment

Although there are no recognised evidence-based protocols for the management of sudden anosmia in a presumed viral infection, general guidelines can be drawn from the current recommendations.

There is a role for the use of empirical oral steroids in idiopathic anosmia to decrease inflammation and oedema [4], but in these cases we do not recommend oral steroids due the increased risks of immunosuppression in the current pandemic.

The use of intranasal steroids seems relatively low risk, however it is unlikely to impact the presumed neurological cause of the anosmia in this syndrome. For those currently taking intranasal steroids with a low bioavailability we recommend continuing on them, but the small risk of exacerbating upper respiratory tract infection with the virus and the low probability of benefit lead us to also recommend against the initiation of intranasal steroid therapy.

Smell training [5] has been demonstrated to have a positive impact on smell recovery in almost every form of smell loss [6,7]. It is safe, simple, uses easily available domestic products and can be done at home, making it an ideal intervention in the midst of social distancing. Full instructions can be found on the AbScent website (www.abscent.org).

Table 1. summary of the case series: patients presenting to the clinician-authors' practice in the last 2 weeks with ISOA.

Age	Gender	Time since onset (weeks)	Other symptoms	Positive test result?	Self isolating?
33	M	3	Mild flu like symptoms lasting <24 hours, no cough or fever, anosmia presented first	Not tested	N – advised no need
39	F	1	Sore throat, fatigue, myalgia, cough, presented at same time	Not tested	Y - telephone consultation
31	F	2	Mild sore throat, presentedat same time	Not tested	N - advised no need
35	F	2	Isolated symptom	Not tested	N
41	M	2	Isolated symptom	Not tested	N
27	M	1	Mild muscle aches, anosmia presented first	Not tested	N
40	M	3	Short episode of fever, anosmia presented soon after	Not tested	N - advised no need
33	M	2	Isolated symptom	Not tested	N
37	M	2	Isolated symptom	Not tested	N
48	M	3	Isolated symptom	positive	Y
50	M	1 day	Isolated symptom as prodrome with myalgia symptoms onset 24hr later	Not tested	Y

Expected recovery

Although it is too early to tell at this moment whether this form of smell loss will follow the pattern of other post viral syndromes [8] it seems likely that the underlying pathological mechanism is the same and a similar pattern of smell recovery, either partial or complete over several months, is to be expected [9]. This is supported by some anecdotal reports from areas already affected by the virus.

Conclusion and recommendations

We posit that there is a heretofore unrecognised syndrome of SARS-CoV-2 infection: Isolated Sudden-Onset Anosmia (ISOA). Current guidelines for self-isolation do not recognise this and at least one of the patients in the case series was given official

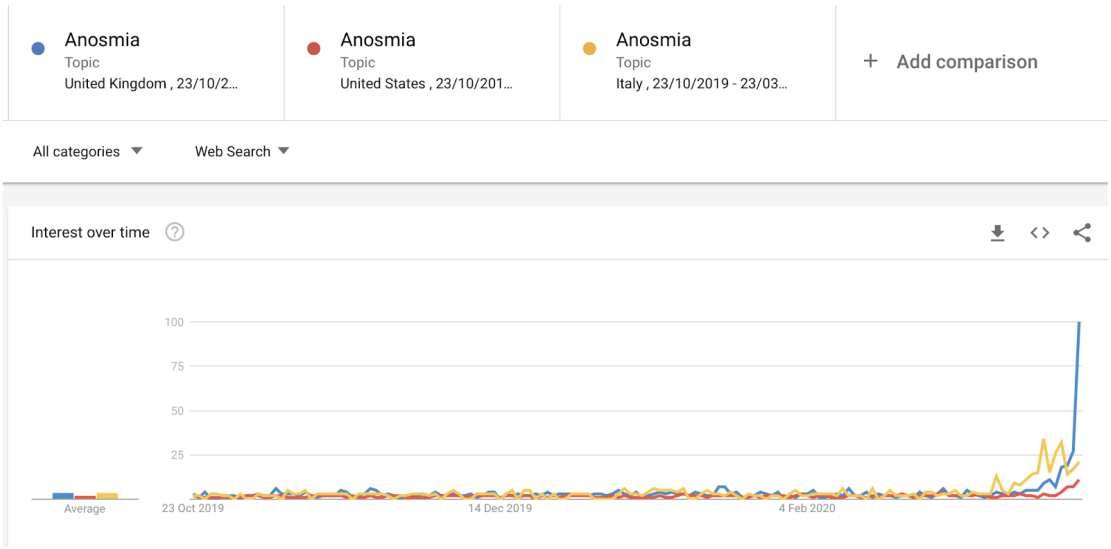

Figure 2. Google trends search terms for the "anosmia" topic since the start of the pandemic in October 2019 for UK (blue), US (red), and Italy (yellow). We attempted to obtain similar numbers for the Chinese search engine Baidu and the social networking site Weibo but this was not possible. Google Trends accessed 23 Mar 2020 (https://trends.google.com).

contradictory advice to return to work which fortunately they did not comply with. They developed a full-blown syndrome within 24 hours of the anosmia, meaning they would have been at work when they would have been at peak infectiousness.

Although we await further, more rigorous evidence of ISOA as a syndrome we feel that the balance of risks is such that treating sudden onset anosmia as a diagnostic symptom of SARS-CoV-2 infection in the current pandemic is warranted. We urge all healthcare practitioners with patients presenting with ISOA to treat these patients as possible COVID-19 positive with appropriate precautions and to avoid prescribing oral immunosuppressants in these cases. We similarly suggest that public health advice be updated with ISOA as the fourth syndrome of SARS-CoV-2.

Authorship contribution

SG wrote the manuscript and provided patient case data, CK provided the data for AbScent membership and edited the manuscript, CH developed the initial manuscript idea, edited the manuscript and provided patient case data.

Conflict of interest

The authors declare no conflicts of interest.

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